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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,482	12/21/2001	Janet A. Warrington	3445	2372

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,482	WARRINGTON ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,17 and 21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,17 and 21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 5/9/05, are acknowledged. Amended claims 1 and 4, cancelled claims 5-16 and 18-20, and new claims 28-32 are acknowledged.

Applicant's arguments, filed 5/9/05, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-4, 17, and 21-32 are herein under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-25 and 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 24-25 and 28-30 are vague and indefinite because it is unclear if the limitations in these claims are method steps or if they are limitations of the system (product). If they are limitations of the system, it is unclear what structural limitations are intended. It is noted that instant claim 4 is acceptable in this regard, because the processor is limited to perform a step. Clarification of these issues via clearer claim wording is requested. Claim 30 is also rejected due to its dependency from instant claim 28.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 17, and 24-31 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e)(1) as being anticipated by Bass et al. (2001/0039014 A1).

Bass et al. disclose amplifying large nucleic acids by PCR in which amplicons of up to 40 kb are generated (paragraph 0235) which encompasses amplicons of 3 to 15 kilobases, as stated in instant claims 28 and 29. Bass et al. disclose automated devices and systems for arraying nucleic acids and for making and copying arrays, for performing in vitro translation and/or transcription of nucleic acid libraries, and for screening (abstract and paragraph 0002). Bass et al. disclose automated systems to assess biological phenomena including gene expression levels in response to stimuli (high throughput DNA genotyping), as well as integrated systems for performing mixing experiments (sample preparation method), DNA amplification (PCR), and DNA sequencing (genotyping) (paragraph 0003), as stated in instant claim 1. Figure 13 shows a DNA fragment preparation device (paragraph 0111). Bass et al. disclose nucleic acid fragments are optionally contacted in a single pool or in multiple pools (paragraphs 0018 and 0058) which represents pooling aliquots of a plurality of amplicons into a plurality of pooled samples. Bass et

al. disclose laboratory attempts to meet increased demand for product development and research with minimal use of laboratory personnel (paragraph 0003). Bass et al. disclose using a nucleic acid shuffling module to dispense elongated nucleic acids into one or more multi-well plates (paragraph 0019) which represents an automated high density probe array loader, as stated in instant claim 1. Bass et al. disclose automated systems with robotics and fluid handling modules such as for microtiter tray manipulation (paragraph 0006) which is reasonably interpreted to be a sample preparation automation system, as stated in instant claims 1 and 2. Bass et al. disclose samples can be treated with at least one disruptive physical condition, such as freeze-thawing, cold-hot cycling (paragraph 0573) which inherently requires a refrigerated unit, as stated in instant claim 31. Bass et al. disclose using a microamplifier in which DNA is placed in a microcapillary and moved through three resistors whose temperatures are programmed (paragraph 0550). Bass et al. disclose using a robotic arm to move the capillary (paragraph 0550). As these modules are part of an integrated system (Figures 1A to 7), the temperate treatment and robotic arm microamplifier are connected with the nucleic acid shuffling module representing the probe array loader. Bass et al. disclose using devices and systems using an array of reaction mixtures that include one or more diversified nucleic acids (i.e. mutagenized or transcribed mutagenized) (paragraph 0010) which represent variation detection (an automated high density probe array loader), as stated in instant claim 1. Bass et al. disclose libraries that involve hybridization to a selected nucleic acid probe (paragraph 0195). Bass et al. disclose using PCR with techniques for rapid genotyping and quantification with hybridization probes (paragraph 0332). Since the probes are for the one or more diversified nucleic acids as described above, Bass et al. disclose a physical array with a set of specified elements (features) arranged in

a specified spatial arrangement and a logical array with a set of specified elements that permits access to the elements of the set (paragraph 0133). As each probe cannot physically be located at the same position, each probe is inherently present in a different feature of the array. Bass et al. disclose using two probes labeled with different fluorophores that transfer energy between them to become excited and detected if a desired genotype is present (paragraphs 0335 and 0336) which represents determining a genotype, as stated in instant claim 1. Bass et al. disclose the devices and integrated systems contain a bar-code sample tracking module which includes a bar code reader and a computer readable database (memory) with bar codes for corresponding arrays (paragraph 0011) which represents an electromagnetic encoding system, as stated in instant claims 1, 3, 17, and 26-27. Bass et al. disclose data obtained by the detection device is processed, stored, and analyzed by a computer system including a microprocessor and memory (paragraph 0423), as stated in instant claims 1 and 4. Bass et al. disclose using PCR to amplify elongated nucleic acids to produce an amplified array of elongated nucleic acids (paragraph 0019) which represents long range PCR amplification, as stated in instant claim 28. Bass et al. disclose various sources of nucleic acids, including cDNA, DNA generated by reverse transcription, and antisense nucleic acid (paragraph 0020), as stated in instant claim 30. Bass et al. disclose simultaneous addition, cleaving and synthesizing of one or more DNA and antisense nucleic acid (paragraphs 0019 and 0070). Bass et al. disclose using nucleic acid fragments up to about 100 bases (paragraph 0238). Bass et al. disclose a nucleic acid shuffling or mutagenesis module which is preceded by a module which allows overlapping of oligonucleotides to be assembled into multimers (paragraph 0014), which represents tiling. Bass et al. disclose selecting, recombining, and re-arraying one or more members (nucleic acid) of an array

(paragraph 0082) which represents a contiguous sequence being tiled on an arrays, as stated in instant claim 25. Bass et al. disclose the analysis device allows one to quantitatively measure the frequency of recombination between DNA polymorphisms in parental genes (paragraph 0554). Bass et al. disclose the use of molecular beacons which are probes that can be used in various amplification reactions that report the presence of specific nucleic acids (region of interest), including the detection of single-nucleotide variations (paragraph 0329) which represents determining the genotype of a plurality of single nucleotide polymorphisms in a region of interest, as stated in instant claims 1, 4, and 24. Bass et al. disclose providing nucleic acids to a system (paragraph 0231) with wash conditions and washing away unlinked strands (paragraphs 0232-0233 and 0483-0484) as well as eluting or isolating materials from the system (paragraphs 0288, 0402, Figure 13), a DNA fragment prep device wherein DNA that binds efficiently to a C18 hydrophobic column and which can be quantitatively eluted and concentrated using the principle of the SEP-PAK C18 column (vacuum assisted) modified for use in an automated device which may include lyophilization (vacuum assisted freeze drying) (paragraph 0549) as well as automated systems that perform repetitive fluid handling operations for transferring material and manipulate conditions such as exposure to air (0005) which represents a vacuum-assisted wash station, as stated in instant claim 1.

Thus, Bass et al. anticipate the limitations in claims 1-4, 17, and 24-31.

Applicants' arguments regarding Bass et al. not teaching a vacuum-assisted wash station is considered unpersuasive due to the passages reiterated below: Bass et al. disclose providing nucleic acids to a system (paragraph 0231) with wash conditions and washing away unlinked

strands (paragraphs 0232-0233 and 0483-0484) as well as eluting or isolating materials from the system (paragraphs 0288, 0402, Figure 13), a DNA fragment prep device wherein DNA that binds efficiently to a C18 hydrophobic column and which can be quantitatively eluted and concentrated using the principle of the SEP-PAK C18 column (vacuum assisted) modified for use in an automated device which may include lyophilization (vacuum assisted freeze drying) (paragraph 0549) as well as automated systems that perform repetitive fluid handling operations for transferring material and manipulate conditions such as exposure to air (0005) which represents a vacuum-assisted wash station, as stated in instant claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21-23 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bass et al. (2001/0039014 A1) as applied to claims 1-4, 17, and 24-31 above, and further in view of Garner et al. (US 20030054388 A1) and Dong et al. (US 6,780,585 B1).

Bass et al. teach the limitations of claims 1-1, 17, and 24-31 as discussed above. Bass et al. do not teach probe arrays with feature sizes of about 20 x 24 microns or smaller (instant claim 21), an array capable of simultaneous screening of 30 kilobases of sense and antisense nucleic acid sequences (instant claim 22), resequencing or variation detection arrays (instant claim 23), or an array comprising 400,000 different sequence probes (instant claim 32).

Garner et al. describe high density arrays with feature sizes of 20 microns (paragraph 0090) and 20 microns or less (paragraph 0100) which represents 20 x 24 microns or smaller, as stated in instant claim 21. Garner et al. describe oligonucleotide probe arrays of greater than 300,000 probes, including 2 million which are independently deposited or created on a substrate (paragraphs 0098 and 0099) which represents 400,000 probes, as stated in instant claim 32. Garner et al. describe using probe arrays for detecting variation (paragraph 0011), as stated in instant claim 23. Garner et al. describe high complexity probes of 50kb or greater for distinct loci to be detected (paragraphs 0038-0040) which represents different probes in the array, as stated in instant claim 32.

Dong et al. describe using large arrays and arrays with probes (col. 2, lines 51-52 and col. 20, lines 7-10). Dong et al. describe the methods allowing for the simultaneous analysis of both

strands (e.g., the sense and antisense strands) and are ideal for multiplexing (col. 11, lines 8-15), as stated in instant claim 22.

Garner et al. state detection techniques of comparative genomic analysis for somatic diseases has expanded to genetic mutations and deletion at both the macroscopic and microscopic level (paragraph 0004). Garner et al. state difficulties in some techniques, such as karyotyping and comparative genomic hybridization including the inability to implement them in a high-throughput or automated assay setting (paragraphs 0006-0008). Dong et al. state electrophoretic separation and analysis in many clinical laboratories would not be technically feasible to accommodate a large number of samples in a cost-effective manner (col. 5, lines 30-40). It would have been obvious to the person of ordinary skill in the art at the time of the invention to provide cost effective, high-throughput methods, as stated by Bass et al. for high resolution mapping for genetic variations, as stated by Bass et al. and Garner et al. with simultaneous screening of sense and antisense strands, as stated by Dong et al. The person of ordinary skill in the art would have been motivated to make these modifications in order to provide detailed mapping necessary for the medical diagnosis of complex diseases (as stated by Garner et al. (paragraph 0010) in a cost-effective manner, as stated by Dong et al. (col. 5, lines 32-35).

Thus, Bass et al. in view of Garner et al. and Dong et al. motivate the instant invention.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
7/22/05

July 11, 2005